



Please type a plus sign (+) inside this box



PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | | | | | |
|---|---|----|---|--------------------------|-------------------------|
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Complete if Known | |
| | | | | Application Number | 09/003,869 |
| | | | | Filing Date | January 7, 1998 |
| | | | | First Named Inventor | Beeley, Nigel |
| | | | | Group Art Unit | 1653 |
| | | | | Examiner Name | Davenport, A.M. Mohamed |
| Sheet | 1 | of | 4 | Attorney Docket Number | 030639.0043 UTL |

TECH CENTER 1600129000

AUG 08 2001

RECEIVED

| U.S. PATENT DOCUMENTS | | | | | | |
|------------------------|------------------|----------------------|--------------------------------------|--|---|--|
| Examiner Initials * | Cite No. 1 | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MMDDYYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | | Number | Kind Code ² (if known) | | | |
| Am ↑ ↓ Am | | 5,118,666 | | Habener | 6/2/92 | 514/12 |
| | | 5,120,712 | | Habener | 6/9/92 | 514/12 |
| | | 5,424,286 | | Eng | 6/13/95 | 514/12 |
| | | 5,512,549 | | Chen | 4/30/96 | 514/12 |
| | | 5,545,618 | | Buckley | 8/13/95 | 514/12 |
| | | 5,574,008 | | Johnson | 11/12/96 | 514/12 |
| | | 5,686,511 | | Bobo | 11/11/97 | 523/412 |

| FOREIGN PATENT DOCUMENTS | | | | | | | | |
|--------------------------|------------------|-------------------------|---------------------|--------------------------------------|--|---|--|----------------|
| Examiner Initials * | Cite No. 1 | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
| | | Office ³ | Number ⁴ | Kind Code ⁵ (if known) | | | | |
| Am | | WO | 9325579 | | Francoeur | 23.12.93 | OK | |
| 7 | | WO | 9318786 | | Efendic | 30.09.93 | OK | |
| 2 | | WO | 9111457 | | Buckley | 08.08.91 | OK | |
| Am | | WO | 9011296 | | Habener | 10.04.90 | OK | |

| | | | |
|-----------------------|-----------------|--------------------|--------|
| Examiner Signature | Abdel A Mohamed | Date Considered | 5/6/02 |
|-----------------------|-----------------|--------------------|--------|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



Please type a plus sign (+) in this box



PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | | | | | |
|---|---|--------------------------|--------------------------------|------------------------|-----------------|
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | Complete if Known | | | |
| | | Application Number | 09/003,869 | | |
| | | Filing Date | January 7, 1998 | | |
| | | First Named Inventor | Beeley, Nigel | | |
| | | Group Art Unit | 1653 | | |
| | | Examiner Name | Davenport, A.M. <i>Mohamed</i> | | |
| Sheet | 2 | of | 4 | Attorney Docket Number | 030639.0043 UTL |

TECH CENTER 1600 2900

AUG 08 2001

RECEIVED

| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | | | |
|---|--------------------------|---|----------------|
| Examiner Initials * | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ² |
| <i>Am</i> | | ADELHORST, K., et al, "Structure-activity studies of glucagon-like peptide-1 (GLP-1)," <i>J. Bio Chem</i> 269(9):6275-8 (1994) | |
| | | BARTLETT, et al, "Inhibition of Chymotrypsin by Phosphonate and Phosphoramidate Peptide Analogs," <i>Bioorg. Chem.</i> 14:356-377 (1986) | |
| | | BHAVSAR, "Inhibition of gastric emptying and of food intake appear to be independently controlled in rodents," <i>Soc. Neurosci. Abst.</i> 21:460 (188.8)(1995) | |
| | | COHEN, et al, <i>The Pico Tag Method: A Manual of Advanced Techniques for Amino Acid Analysis</i> , pp. 11-52, Millipore Corporation (1989) | |
| | | D'ALESSIO et al. "Elimination of the Action of glucagon-like Peptide 1 Causes an Impairment of glucose tolerance after Nutrient Ingestion by Healthy Baboons," <i>J. Clin. Invest.</i> , 97:133-38, 1996 | |
| | | EISSELE et al. "Rat Gastric somatostatin and Gastrin Release: Interactions of Exendin-4 and Truncated Glucagon-Like Peptide-1 (GLP-1) Amide," <i>Life Sci.</i> , 55:629-34, 1994 | |
| | | ENG et al. "Isolation and Characterization of Exendin-4, an Exendin-3 Analogue, from <i>Heloderma suspectum</i> Venom", <i>J. Biol. Chem.</i> , 267:7402-05, 1992 | |
| | | ENG et al. "Purification and Structure of Exendin-3, a New Pancreatic Secretagogue Isolated from <i>Heloderma horridum</i> Venom," <i>J. Biol. Chem.</i> , 265:20259-62, 1990 | |
| | | FEHMANN et al. "Stable Expression of the Rat GLP-I Receptor in CHO Cells: Activation and Binding Characteristics Utilizing GLP-I(7-36)-Amide, Oxynomodulin, Exendin-4, and Exendin(9-39)," <i>Peptides</i> 15 (3): 453-6, 1994 | |
| | | FERGUSON et al. "Cell-Surface Anchoring of Proteins Via Glycosylphosphatidylinositol Structures", <i>Annu. Rev. Biochem.</i> 57:285-320 (1988) | |
| | | GOKE et al. "Exendin-4 Is a High Potency Agonist and Truncated Exendin-(9-39)-amide an Antagonist at the Glucagon-like Peptide 1-(7-36)-amide Receptor of Insulin-secreting -Cells", <i>J. Biol. Chem.</i> , 268:19650-55, 1993 | |
| <i>Am</i> | | HALAAS, J.L., et al, "Weight-Reducing Effects of the Plasma Protein Encoded | |

| | | | |
|-----------------------|-------------------------|--------------------|---------------|
| Examiner Signature | <i>Abdel A. Mohamed</i> | Date Considered | <i>5/6/02</i> |
|-----------------------|-------------------------|--------------------|---------------|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Unique citation designation number. ²Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



Please type a plus sign (+) inside this box



PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Project of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | | | |
|---|--------|--------------------------|--------------------------------|
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | Complete if Known | |
| | | Application Number | 09/003,869 |
| | | Filing Date | January 7, 1998 |
| | | First Named Inventor | Beeley, Nigel |
| | | Group Art Unit | 1653 |
| | | Examiner Name | Davenport, A.M. <i>Mohamed</i> |
| Sheet | 3 of 4 | Attorney Docket Number | 030639.0043 UTL |

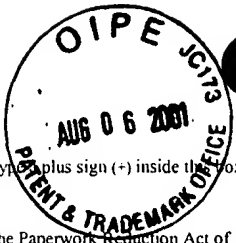
| | | |
|-----------|--|--|
| | by the obese Gene," <u>Science</u> 269:543-546 (1995) | |
| <i>Am</i> | KODAMA, J., et al, "Effect of Captopril on Glucose Concentration Possible Role of Augmented Postprandial Forearm Blood Flow," <u>Diabetes Care</u> 13(11):1109-1111 (1990) | |
| <i>↑</i> | KOLLIGS, et al, "Reduction of the incretin effect in rats by the glucagon-like peptide-1 receptor antagonist exendin (9-39) amide," <u>Diabetes</u> 44:16-19 (1995) | |
| | LEIBEL, R.L., et al, "Changes in Energy Expenditure Resulting from Altered Body Weight," <u>New England Journal of Medicine</u> 332(10):621-628 (1995) | |
| | LITHELL, et al, "Insulin Sensitivity in Newly Detected Hypertensive Patients: Influence of Captopril and Other Antihypertensive Agents on Insulin Sensitivity and Related Biological Parameters," <u>J. Cardiovasc. Pharmacol.</u> 15 (Supp 5):S46-S52 (1990) | |
| | MALHOTRA et al. "Exendin-4, a new peptide from <i>Heloderma suspectum</i> venom, potentiates cholecystokinin-induced amylase release from rat pancreatic acini", <u>Regulatory Peptides</u> , 41:149-56, 1992 | |
| | MONTROSE-RAFIZADEH et al. "Structure-function Analysis of Exendin-4 / GLP-1 Analogs", <u>Diabetes</u> , 45(Suppl. 2):152A, 1996 | |
| | O'HALLORAN et al. "Glucagon-like peptide-1 (7-36)-NH ₂ : a physiological inhibitor of gastric acid secretion in man," <u>J Endocrinol</u> 126 (1): 169-73 (1990) | |
| | ØRSKOV et al. "Biological Effects and Metabolic Rates of Glucagonlike Peptide-1 7-36 Amide and glucagonlike Peptide-1 7-37 in Healthy Subjects Are Indistinguishable", <u>Diabetes</u> , 42:658-61 (1993) | |
| | PELLEYMOUNTER, et al, "Effects of the obese Gene Product on Body Weight Regulation in ob/ob Mice," <u>Science</u> 269:540-543 (1995) | |
| | RAUFMAN et al. "Truncated Glucagon-like Peptide-1 Interacts with Exendin Receptors in Dispersed Acini from Guinea Pig Pancreas", <u>J. Biol. Chem.</u> 267:21432-37 (1992) | |
| <i>✓</i> | RAUFMAN et al. "Exendin-3, a Novel Peptide from <i>Heloderma horridum</i> Venom, Interacts with Vasoactive Intestinal Peptide Receptors and a Newly Described Receptor on dispersed Acini from Guinea Pig Pancreas," <u>J. Biol. Chem.</u> 266:2897-902 (1991) | |
| <i>Am</i> | SCHEPP et al. "Exendin-4 and exendin-(9-39)NH ₂ : agonist and antagonist, respectively, at the rat parietal cell receptor for glucagon-like peptide-1-(7- | |

| | | | |
|--------------------|-------------------------|-----------------|---------------|
| Examiner Signature | <i>Abdel A. Mohamed</i> | Date Considered | <i>5/6/02</i> |
|--------------------|-------------------------|-----------------|---------------|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Unique citation designation number. ²Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



Please type plus sign (+) inside the box



PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | | | | | |
|---|---|--------------------------|--------------------------------|------------------------|-----------------|
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | Complete if Known | | | |
| | | Application Number | 09/003,869 | | |
| | | Filing Date | January 7, 1998 | | |
| | | First Named Inventor | Beeley, Nigel | | |
| | | Group Art Unit | 1653 | | |
| | | Examiner Name | Davenport, A.M. <i>Mohamed</i> | | |
| Sheet | 4 | of | 4 | Attorney Docket Number | 030639.0043 UTL |

TECH CENTER 1561/2900

AUG 08 2001

RECEIVED

| | | | |
|-----------|--|---|--|
| | | 36)NH ₂ ," <u>Eur. J. Pharm.</u> 269:183-91 (1994) | |
| <i>Am</i> | | SCHJOLDAGER et al. "GLP-1 (Glucagon-like Peptide 1) and Truncated GLP-1, Fragments of Human Proglucagon, Inhibit Gastric Acid Secretion in Humans," <u>Dig Dis Sci</u> 34 (5): 703-8 (1989) | |
| | | SINGH et al. "Use of ¹²⁵ I-[Y ³⁹]exendin-4 to characterize exendin receptors on dispersed pancreatic acini and gastric chief cells from guinea pig," <u>Regul. Pept.</u> 53:47-59 (1994) | |
| | | THORENS, "Expression cloning of the pancreatic cell receptor for the glucocretin hormone glucagon-like peptide 1," <u>Proc. Natl. Acad. Sci. USA</u> 89:8641-45 (1992) | |
| | | THORENS, et al. "Cloning and Functional Expression of the Human Islet GLP-1 Receptor," <u>Diabetes</u> 42 (11): 1678-82 (1993) | |
| | | TURTON, et al, "A role for glucagon-like peptide-1 in the central regulation of feeding," <u>Nature</u> 379:69-72 (1996) | |
| | | VEALE, P.R., et al, "The presence of islet amyloid polypeptide/calcitonin generated peptide/salmon calcitonin binding sites in the rat nucleus accumbens," <u>European Journal of Pharmacology</u> 262:133-141 (1994) | |
| | | WANG et al. "Glucagon-like Peptide-1 Is a Physiological Incretin in Rat," <u>J. Clin. Invest.</u> , 95:417-21 (1995) | |
| | | WATSON, N., et al, "Effects of captopril on glucose tolerance in elderly patients with congestive cardiac failure," <u>Current Medical Research and Opinion</u> 12(6):374-378 (1991) | |
| | | WETTERGREN et al. "Truncated GLP-1 (Proglucagon 78-107-Amide) Inhibits Gastric and Pancreatic Functions in Man," <u>Dig Dis Sci</u> 38 (4): 665-73 (1993) | |
| | | WILLMS et al. "Gastric Emptying, Glucose Responses, and Insulin Secretion after a Liquid Test Meal: Effects of Exogenous Glucagon-Like Peptide-1 (GLP-1)-(7-36) Amide in Type 2 (Noninsulin-Dependent) Diabetic Patients," <u>J. Clin. Endocrinol. Metab.</u> 81(1):327-32 (1996) | |
| <i>Am</i> | | YOUNG, et al, <u>Program and Abstracts, 10th International Congress of Endocrinology</u> June 12-15, 1996, San Francisco, p. 419 (P2-58) | |

| | | | |
|--------------------|-------------------------|-----------------|---------------|
| Examiner Signature | <i>Abdel A. Mohamed</i> | Date Considered | <i>5/6/02</i> |
|--------------------|-------------------------|-----------------|---------------|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Unique citation designation number. ²Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box

FEB 11 2002

PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

| | | | | |
|---|---|----|------------------------|------------------|
| Substitute for form 1449A/PTO | | | Complete if Known | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | Application Number | 09/003,869 |
| | | | Filing Date | January 7, 1998 |
| | | | First Named Inventor | Arnold Beeley |
| | | | Group Art Unit | 1653 |
| | | | Examiner Name | A. Davenport |
| | | | Attorney Docket Number | 030639.0043.CPA1 |
| Sheet | 1 | of | 1 | |

| U.S. PATENT DOCUMENTS | | | | | | |
|--------------------------------|-----------------------|----------------------|-----------------------------------|---|--|---|
| Examiner Initials ¹ | Cite No. ¹ | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | | Number | Kind Code ² (if known) | | | |
| Am | AA | 6,191,102 | B1 | DiMarchi et al. | 02/20/2001 | 514/2 |
| | | | | | | |
| | | | | | | |
| | | | | | | |

| FOREIGN PATENT DOCUMENTS | | | | | | | |
|--------------------------------|-----------------------|-------------------------|---------------------|-----------------------------------|---|--|---|
| Examiner Initials ¹ | Cite No. ¹ | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | | Office ³ | Number ⁴ | Kind Code ⁵ (if known) | | | |
| Am | AB | WO | 98/05351 | A1 | Amylin Pharmaceuticals, Inc. | 02/12/1998 | |
| | AC | WO | 98/19698 | A1 | Eli Lilly and Company | 05/14/1998 | |
| | AD | WO | 98/30231 | A1 | Amylin Pharmaceuticals, Inc. | 07/16/1998 | |
| Am | AE | WO | 99/07404 | A1 | Amylin Pharmaceuticals, Inc. | 02/18/1999 | |

| NON PATENT LITERATURE DOCUMENTS | | | | |
|---------------------------------|-----------------------|---|--|--|
| Examiner Initials ¹ | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | | |
| | | | | |
| | | | | |

| | | | |
|--------------------|------------------|-----------------|--------|
| Examiner Signature | Abdel A. Mohamed | Date Considered | 5/6/02 |
|--------------------|------------------|-----------------|--------|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation is not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.